the claim." Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569,1574, 224 USPQ 409,412 (Fed. Cir. 1984). See also, In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893 (CCPA 1963). Although the claims were amended to remove "consisting essentially of" in response to the Examiner's rejections as based on what Applicants consider to be an erroneous interpretation of the transitional phrase, Applicants note for the record their objection to this interpretation, and reserve the right to prosecute claims having the term "consisting essentially of," or the like, in future applications.

Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 2, 5, 7, 9, 14 and 76-83 under 35 U.S.C. § 112, first paragraph for lack of an adequate written description. Although Applicants believe that the rejection is not supported by the case law cited by the Examiner (which cases pertain to completely unknown gene sequences and not amino acid sequences having limited modifications), the claim amendments made herewith are believed to obviate the rejection. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. 112, first paragraph.

Rejections Under 35 U.S.C. § 102

1. The Examiner rejected claims 2, 9, 76, and 80-82 under 35 U.S.C. § 102(b) as anticipated by the Fikes PCT application (WO95/04542).

Applicants have amended claims 2 and 9 to further define the amino acid sequence of the HLA class II binding peptide. As amended, Applicants claim a peptide that consists of EYVIKVSARVRF (SEQ ID NO:7), or a functional variant that differs from SEQ ID NO:7 by one amino acid deletion addition or substitution; each of the foregoing can further consist of 0-10 amino acids added to either or both ends of the respective amino acid sequence. Therefore, the claimed peptide has a maximum size of 33 amino acids (12 amino acids of SEQ ID NO:7 + 1 amino acid for the functional variant + 20 amino acids for the additions to both ends) and a minimum size of 11 amino acids (12 amino acids of SEQ ID NO:7 - 1 amino acid deletion for the functional variant).

The portion of Fikes (WO 95/04542) cited by the Examiner (page 14, last paragraph through page 16, and claim 8) describes a nucleic acid molecule that encodes a particular

fragment of MAGE-1, specifically the 58 amino acid C-terminal fragment. No other fragments are described by Fikes. Thus Fikes does not teach the peptide claimed in claim 2, or any other of the claims as amended.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(b).

2. The Examiner rejected claims 2, 9 and 80 under 35 U.S.C. § 102(b) as anticipated by the Topalian PCT application (WO97/11669).

The sections of the Topalian PCT application cited by the Examiner relate to a method for screening melanoma antigens for the presence of HLA class II tumor associated antigens, including the MAGE-1 melanoma antigen. The amendments to the claims obviate the rejection based on Topalian, because Topalian does not even identify which portion of MAGE-1 might contain a HLA class II binding peptide. In contrast, Applicants are claiming specific peptides of the specific recited sequences that bind HLA DRB1*15. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(b).

3. The Examiner rejected claim 2 under 35 U.S.C. § 102(a) as anticipated by the Chaux et al. reference.

The Chaux paper recites HLA class II binding peptides of a different MAGE protein, MAGE-A3. Because the claim amendment proposed above restricts the MAGE-A1 HLA DRB1*15 binding peptide sequence to SEQ ID NO:7 with one possible amino acid substitution and 0-10 amino acid additions at either or both ends, the peptides provided in the Chaux reference do not anticipate the claimed invention. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(e).

4. The Examiner rejected claims 2, 5, 7, 9, 14, 78-80 and 83 under 35 U.S.C. § 102(a) as anticipated by the Thielemans PCT application (WO99/14326).

Applicants have amended the claims to clarify the scope of functional variants as claimed. The Thielemans application does not disclose a functional variant of the MAGE-A1 peptide as now claimed. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(a).

5. The Examiner rejected claims 2, 5, 7, 78 and 79 under 35 U.S.C. § 102(e) as anticipated by the Chaux patent (US 5,965,535).

Chaux does not disclose functional variants as now claimed in the instant application. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(e).

Rejections Under 35 U.S.C. § 103

1. The Examiner rejected claims 2, 9, 76, 77, 80-82 under 35 U.S.C. § 103 as unpatentable over WO95/04542 (Fikes et al.).

The Examiner has based this rejection on the teaching of a peptide comprising SEQ ID NO:7 in the Fikes PCT application. Applicants agree that Fikes teaches a particular peptide consisting of the C-terminal 58 amino acids of MAGE-A1 (depicted in the last paragraph of page 4 of Fikes). Fikes also teaches, in claim 3, a peptide that consists of 9 of the 12 amino acids of SEQ ID NO:7 of the instant application. As noted by the Examiner, the peptide of Fikes (SEQ ID NO:8) is missing the first amino acid (E) and the last two amino acids (R, F) of SEQ ID NO:7 of the present application. Applicants agree that Fikes teaches this specific peptide.

The Examiner also points to the section of the Fikes application (page 5, third full paragraph) in which Fikes teaches that the peptide can be optionally modified and/or flanked by additional amino acid residues. The Examiner seeks to establish that this paragraph provides motivation for one of ordinary skill in the art to have made the invention now claimed.

Applicants disagree, particularly because Fikes does not teach which amino acids, or how many amino acids, should be added to the peptide. Whether or not Fikes provides a general motivation to one of ordinary skill in the art to add amino acids to the ends of a peptide, Fikes does not provide the motivation required for a finding of obviousness. The Examiner must demonstrate a specific motivation to make the peptide now claimed by Applicants, e.g., Fikes must have taught that the addition of specific amino acids to a specific peptide was desirable. In re Werner Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) ("[A] rejection cannot be predicated on the mere identification ... of individual components of claimed limitations. Rather, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in

the manner claimed.") The Examiner has not indicated why a skilled artisan, without knowledge of the claimed HLA DRB1*15 binding peptide, would have selected one particular peptide from among the many disclosed in the Fikes PCT application, and why the skilled artisan would have modified such a peptide to obtain the peptide now claimed. Accordingly, the proper showing to support an obviousness rejection has not been provided.

Moreover, even if the Examiner is able to provide an appropriate showing that specific motivation existed for one of ordinary skill in the art to alter a peptide presented in the PCT application, Fikes does not teach which amino acids to add, to which peptide listed in the application. The only recitation of alterations that can be made to peptides is a general recitation that the peptides "can be optionally flanked and/or modified...." This general recitation by Fikes of potential modifications to the peptides disclosed is not sufficient to support a finding of obvlousness.

In addition, Fikes states that the peptide induces a CTL response (page 5, third full paragraph, last sentence) via MHC class I molecules. In contrast, Applicants have claimed peptides that bind class II molecules (DRB1*15 specifically), and thus would be expected to induce a helper T cell response, not a CTL response. Thus Fikes teaches away from modifying the disclosed peptide sequences in a manner that produces a class II binding peptide. At the very least, this passage is a further reflection on the lack of motivation to make the specific HLA DRB1*15-binding peptides now claimed by Applicants.

Furthermore, with respect to the particular peptide that would have to be modified to obtain the claimed invention, Fikes taught that SEQ ID NO:8 was an immunogenic peptide (in claim 3), and thus one of ordinary skill in the art would not be motivated to add any amino acids to both ends. Moreover, as stated above, there certainly was not any motivation to add the correct number of amino acids to the correct ends of SEQ ID NO:8. Further, there was no suggestion by Fikes to add the specific amino acids contained in SEQ ID NO:7, and thus Applicants maintain that one of ordinary skill in the art would not have been motivated to do so.

Thus the Examiner has not supplied any motivation or reason why one of ordinary skill in the art would select the claimed peptides from among all of the potential peptide modifications suggested by Fikes. In essence, the Examiner appear to be suggesting that the claimed invention was obvious to try based on the prior art. "Obvious to try," however, is not a proper and

legitimate standard for unpatentability, and does not constitute obviousness. In re Fine, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988).

In summary, Fikes does not provide the specific and clear motivation required under the law to make the specific number and kind of substitutions that would be required to obtain the claimed invention. The Examiner has not indicated any other source for motivation to modify the teachings of Fikes to obtain the claimed invention. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of the claims under 35 U.S.C. § 103 based on WO95/04542 (Fikes et al.).

2. The Examiner rejected claims 5, 14, 78 and 83 under 35 U.S.C. § 103 as unpatentable over Fikes et al. (WO95/04542) in combination with Sanderson et al.

This rejection is similar to the previous Fikes obviousness rejection with the addition of the Sanderson reference to teach the Ii invariant chain for targeted fusions. As above, one of ordinary skill in the art would not have been motivated to add the correct number and kind of amino acids to arrive at the claimed peptides. Sanderson does not cure the essential deficiency of Fikes.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of the claims under 35 U.S.C. § 103 based on WO95/04542 (Fikes et al.) in combination with Sanderson et al.

3. The Examiner rejected claims 2, 5, 9, 14, 78, 80 and 83 under 35 U.S.C. § 103 as unpatentable over WO97/11669 (Topalian et al.) in combination with Sanderson et al.

This rejection is based on the combination of Topalian (for functional variants of SEQ ID NO:7) and Sanderson (for Ii). Based on the claim amendments and arguments set forth above for the Topalian anticipation rejection, Applicants respectfully request that the Examiner withdraw this rejection of the claims under 35 U.S.C. § 103.

4. The Examiner rejected claims 7 and 79 under 35 U.S.C. § 103 as unpatentable over WO95/04542 (Fikes et al.) in view of US patent 6,043,347 (Gelder et al.). The Examiner also rejected claims 1, 2, 5, 9, 11, 14, 78, 80 and 83 over WO97/11669 (Topalian et al.) in view of US

patent 6,043,347 (Gelder et al.). Applicants assume that claims 1 and 11 were not meant to be included in the rejection as these claims were canceled in the previous amendment.

These rejections are based on the previous Fikes or Topalian obviousness rejections with the addition of the Gelder reference to teach D-amino acids. Based on the claim amendments and arguments set forth above for the respective Fikes and Topalian rejections, Applicants respectfully request that the Examiner withdraw this rejection of the claims under 35 U.S.C. § 103.

In view of the amendments and the arguments presented above, Applicants respectfully request that the rejections of the claims be withdrawn. If the Examiner wishes to expedite the prosecution of this application in any way, then the Examiner is invited to contact the Applicants' representative at the telephone number listed below.

Respectfully submitted,

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Amended Claims

2.(twice amended) An isolated HLA [class II] DRB1*15-binding peptide consisting [essentially] of

the amino acid sequence set forth as SEQ ID NO:7, or a functional variant thereof [comprising] consisting of one amino acid addition, substitution or deletion, and

0-10 amino acids added to either or both ends of the amino acid sequence set forth as SEQ ID NO:7, or the functional variant thereof consisting of one amino acid addition, substitution or deletion.

5.(twice amended) The isolated HLA [class II] DRB1*15-binding peptide of claim 2 wherein the isolated peptide comprises an endosomal targeting signal.

7.(twice amended) The isolated HLA [class II] DRB1*15-binding peptide of claim 2 wherein the isolated peptide is non-hydrolyzable.

9.(twice amended) A composition comprising an isolated MAGE-A1 HLA class I-binding peptide and an isolated MAGE-A1 HLA [class II] DRB1*15-binding peptide, wherein the isolated HLA class II-binding peptide consists [essentially] of

the amino acid sequence set forth as SEQ ID NO:7, or a functional variant thereof [comprising] consisting of one amino acid addition, substitution or deletion, and

0-10 amino acids added to either or both ends of the amino acid sequence set forth as SEQ ID NO:7, or the functional variant thereof consisting of one amino acid addition, substitution or deletion.

14.(amended) The composition of claim 9 wherein the isolated MAGE-A1 HLA [class II] DRB1*15-binding peptide comprises an endosomal targeting signal.

76.(twice amended) The isolated HLA [class II] DRB1*15-binding peptide of claim 2 wherein the isolated peptide consists [essentially] of an amino acid sequence selected from the group

consisting of SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:7, or a functional variant thereof consisting of one amino acid addition, substitution or deletion.

77.(amended) The isolated HLA [class II] DRB1*15-binding peptide of claim 2 wherein the isolated peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

78.(amended) The isolated HLA [class II] DRB1*15-binding peptide of claim 5 wherein the endosomal targeting signal comprises an endosomal targeting portion of human invariant chain Ii or LAMP-1.

79.(amended) The isolated HLA [class II] DRB1*15-binding peptide of claim 7 wherein the isolated peptide is selected from the group consisting of peptides comprising D-amino acids, peptides comprising a -psi[CH_2NH]-reduced amide peptide bond, peptides comprising a -psi[$COCH_2$]-ketomethylene peptide bond, peptides comprising a -psi[CH(CN)NH]-(cyanomethylene)amino peptide bond, peptides comprising a -psi[$CH_2CH(OH)$]-hydroxyethylene peptide bond, peptides comprising a -psi[CH_2O]-peptide bond, and peptides comprising a -psi[CH_2S]-thiomethylene peptide bond.

80.(amended) The composition of claim 9 wherein the MAGE-A1 HLA class I-binding peptide and the MAGE-A1 HLA [class II] DRB1*15-binding peptide are combined as a polytope polypeptide.

81.(twice amended) The composition of claim 9 wherein the isolated MAGE-A1 HLA [class II] DRB1*15-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7, or a functional variant thereof consisting of one amino acid addition, substitution or deletion.

82.(twice amended) The composition of claim 9 wherein the isolated MAGE-A1 HLA [class II] DRB1*15-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.